Post-Marketing Safety Surveillance for Human Papillomavirus Vaccine (GARDASIL®)

John Iskander MD MPH
LCDR, U.S. Public Health Service
Immunization Safety Office (ISO)
Office of the Chief Science Officer
Centers for Disease Control and Prevention

General Template for Safety Monitoring of New Vaccines

- Summary of pre-licensure safety data
- Identified or uncertain risks from phase III trials
- Review of any available post-marketing data
- VAERS monitoring plan
- VSD plan: key outcomes for Rapid Cycle Analysis (RCA), other planned studies
- Identification/creation of key case definitions
- Identification of candidate CISA protocols
- Identification of need for special studies

Vaccine Adverse Event Reporting System (VAERS)

- National passive surveillance system for reporting adverse events
- Co-managed by CDC and FDA
- Accepts reports from physicians, other health care providers, and the public
- VAERS advantages:
  - Voluntary
  - Easy to report an adverse event
  - Nationwide reach

VAERS Objectives

- Signal detection
  - Previously unrecognized and/or rare reactions
- Monitoring known reactions
- Identifying pre-existing risk factors that may promote reactions
- Vaccine lot surveillance

Monitoring Reports after Receipt of GARDASIL®

- CDC/FDA researchers will review reports of serious adverse event reports (SAEs) including other medically important conditions (OMIC)
  - Daily alerts will include:
    - Age at vaccination
    - Onset interval (days)
    - Gender
    - Vaccine(s) given
    - Symptom text describing the adverse event, pre-existing medical conditions, and known allergies
- Congenital anomalies are defined in federal regulations as a serious outcome (21 CFR 600.80)
  - Such reports will be included in priority report alerts and will be subject to follow-up (i.e. record review)

Vaccine Safety Datalink (VSD)

- Collaboration: CDC and Managed Care Organizations (MCOs) in the US
- 8 participating MCOs
  - Annual birth cohort > 90,000
- Advantages of VSD for vaccine safety research
  - Large, well-defined population
  - Computerized, linkable administrative data files
  - Powerful tool for controlled population-based studies

Post-marketing Safety Surveillance Activities of GARDASIL® for VSD

- Rapid cycle analysis (RCA)
- VSD database of pregnancy outcomes after vaccination

VSD RCA for GARDASIL®

- Monitor the following outcomes:
  - Hypertension:
    - New diagnoses; ER visits
  - Immediate Hypersensitivity
- Evaluate other pre-specified conditions and associations identified from:
  - VAERS
  - Phase III and IV studies (manufacturer)

VSD RCA for GARDASIL®

- Proposed Methods:
  - Newly developed RCA allows VSD to conduct “real time” monitoring of new vaccines
  - Study design:
    - Women who receive GARDISIL® vaccine
    - Proposed exposure window: 30 days after vaccination
    - Automated outcomes data with chart validation
  - Sequential statistical testing
    - Rates of pre-specified outcomes after GARDISIL ® compared with expected rates

VSD Database of Pregnancy Outcomes after Vaccination

- Objective:
  - To create an analytic database to serve as a resource for measuring the risk of adverse pregnancy outcomes after inadvertent vaccination of pregnant women

VSD Database of Pregnancy Outcomes after Vaccination

- Proposed methods:
  - Create analytic database to be examined on an annual basis
  - All women who were or became pregnant when vaccinated
  - Vaccines of interest:
    - All new vaccines, including HPV vaccine
    - All live viral vaccines
    - Vaccines in which reproductive outcome concerns have been raised
  - Outcomes of interest:
    - Spontaneous abortion
    - Elective termination
    - Still births
    - Live Births
      - Congenital Anomalies

Thank You